ANDA 74-819

Purepac Pharmaceutical Co.
Attention: Joan Janulis
200 Elmora Avenue
Elizabeth, NJ 07207

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Etodolac Tablets, 400 mg

DATE OF APPLICATION: January 31, 1996

DATE OF RECEIPT: January 31, 1996

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

James Wilson
Consumer Safety Officer
(301) 594-0310

Sincerely yours,

Jerry Phillips
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 74-819
cc: DUP/Jacket
Division File
Field Copy
HFD-600/Reading File
HFD-82
HFD-615/MBennett
Endorsement: HFD-615/PRickman, Chief, RSB_____date
HFD-615/WRussell, CSO_____date
HFD-623/ARudman, Sup. Chem_____date
WP File\x:\new\firmsnz\Purepac\ltrs&rev\74819ac.f
F/T hrw 2-22-96
ANDA Acknowledgement Letter!

D, V

ANDA 74-819

Purepac Pharmaceuticals Co.
Attention: Joan Janulis
200 Elmore Avenue
Elizabeth NJ 07207

JUN 12 1996

Dear Madam:

Reference is made to the Abbreviated New Drug Application submitted on January 31, 1996, for Etodolac Tablets 400 mg.

The Office of Generic Drugs has reviewed the bioequivalence data submitted and the following comments are provided for your consideration:

The dissolution testing method used, is different from the FDA recommended methodology. Please submit comparative dissolution for the test and reference listed drug using the following method.

Apparatus:	USP Basket
RPM:	100
Medium:	pH 7.5 Phosphate Buffer, 0.05 M
Volume:	1000 mL
Sampling Times:	5, 10, 20, and 30 minutes
No. of Dosage Units:	12 Test vs. Reference Product (Lodine®, Wyeth-Ayerst)
Q:	NLT in 30 minutes

As described under 21 CFR 314.96 an action which will amend this application is required. The amendment will be required to address all of the comments presented in this letter. Should you have any questions, please call Jason A. Gross, Pharm.D., at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation
and Research

ANDA 74-819

Purepac Pharmaceutical Company
Attention: Elizabeth Trowbridge
200 Elmora Avenue
Elizabeth, NJ 07207

DEC 3 1996

Dear Madam:

Reference is made to your abbreviated new drug application dated January 31, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Etodolac Tablets, 400 mg.

Reference is also made to your amendments dated August 2, September 20, and October 25, 1996.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is **tentatively approved.** This determination is contingent upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product), and is therefore subject to change on the basis of new information that may come to our attention. The listed reference drug product upon which you have based your application is subject to a period of patent protection and therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(4)(B) of the Act until the period has expired, i.e., February 28, 1997.

Please provide the Agency, at least 60 days prior to February 28, 1997, an amendment to this application. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as labeling, chemistry, manufacturing, and controls data as appropriate. An amendment should be submitted even if none of these changes were made. This submission should be designated as a MINOR AMENDMENT in your cover letter. In addition to, or instead of, the amendment requested above, the Agency may, at any time prior to the final date of approval, request that you submit an amendment containing the information described above.

Failure to submit such an amendment requested by the Agency will prompt a review of the application which may result in rescission of this tentative approval letter.

Any significant changes in the conditions outlined in this abbreviated application requires Agency approval before the changes may be made effective.

Prior to issuance of the final approval letter by the Agency, your product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list, published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to February 28, 1997, you should amend your application accordingly.

At the time you submit any amendments, you should contact, Mr. James Wilson, III, Project Manager, at (301) 594-0310 for further instructions.

The introduction or delivery for introduction into interstate commerce of the drug before the effective approval date is prohibited under 21 U.S.C. 331 (d).

Sincerely yours,

Roger L. Williams, M.D.
Deputy Center Director for Pharmaceutical Science
Center for Drug Evaluation and Research

ANDA 74-819

Purepac Pharmaceutical Co.
Attention: Mitchell G. Clark
200 Elmora Avenue
Elizabeth, NJ 07207

JUN 28 1996

Dear Sir:

This is in reference to your abbreviated new drug application dated January 31, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Etodolac Tablets, 400 mg.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies

1. Please identify the in your Etodolac , lot #9540140, at respectively (page 002720).

2. The lot numbers provided on the same batch of COAs by your firm and the manufacturer, are 827959 and 832105 respectively (pages 002773 and 002776). Please explain the lot number inconsistency for the same batch of material.

3. You indicated on page 002957 that prior to packaging, microbiological testing was conducted on the finished product of test batch, lot #PI-888, because the water used in of this test batch contained

This practice of conducting microbiological evaluation is not acceptable. You have manufactured a drug product with a raw material, Purified Water, that was Please be advised that in accordance with 21 CFR 211.84 (d)(4)(5)(6)(e), all materials must meet appropriate written specifications including microbial evaluation where appropriate, before they are approved and released for use in the manufacture of a drug product. Please revise your Purified Water test specification to include In addition please confirm that was not isolated

from your Etodolac Tablets biobatch, lot #PI-888. We strongly recommend that you monitor all including in your purified water system.

4. is not referenced in your FDA 356h form. Please re-submit this form to include the missing information.

5. Please be advised that is currently deficient and the DMF holder is being advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

Please be advised that all DMF(s) referenced in this ANDA have to be found satisfactory at the time of approval of the ANDA. Some of the DMF holders may have to be inspected by our Division of Manufacturing and Product Quality. Any unsatisfactory review/evaluation will delay the approval of the ANDA. You are thus advised to withdraw any DMF references which are unnecessary to support the ANDA.

B. Labeling Deficiencies

1. CONTAINER: 400 mg - 100's, 500's and 1000's

Satisfactory in draft.

2. INSERT

a. DESCRIPTION

i. Revise the third paragraph to read as follows:

Each tablet, for oral administration, contains 400 mg of etodolac. In addition, each tablet contains the following inactive ingredients ...

ii. We note you have listed lactose twice as an inactive ingredient, (lactose and lactose monohydrate). If the lactose used in is "lactose monohydrate" delete the reference to lactose. If not, please specify the type of lactose. We refer you to USP 23 for further guidance.

b. ADVERSE REACTIONS

i. Incidence less than 1% - Probably Causally Related (Adverse reactions reported only in

worldwide postmarketing experience, not seen in clinical trials, are considered rarer and are italicized):

A) Cardiovascular system

Cardiovascular system - Hypertension, ...syncope, *vasculitis (including necrotizing and allergic)*. [Note italic print].

B) Digestive system

Digestive system - Thirst, ... and/or perforation), *intestinal ulceration, pancreatitis*. [Note italic print]

Please revise your labels and labeling, as instructed above, and submit in final print. Please note that we reserve the right to request further changes in your labels and labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with the differences annotated and explained.

In addition to responding to these deficiencies, please note and acknowledge the following in your response:

A. Since there is no official USP monograph for this finished drug product or the drug substance raw material, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be picked up by the FDA at the appropriate time.

B. Please describe the pharmaceutical function of all the excipients used in the formulation of Etodolac tablets, 400 mg.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MINOR amendment and should be so designated in your cover letter. You will be notified in a

separate letter of any deficiencies identified in the bioequivalence portion of your application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #74-819
ANDA #74-819/DUP/Division File
Field Copy
HFD-600/Reading file

Endorsements:

HFD-623/J.Fan/6-10-96
HFD-623/V.Sayeed, Ph.D./6-6-96
HFD-617/J.Wilson, CSO/6-7-96
HFD-613/J.White/C.Park for/6-12-96
HFD-613/J.Phillips/A.Vezza for/6-13-96
X:\NEW\FIRMSNZ\PUREPAC\LTRS&REV\74819N1.NAD
F/T by: bc/6-14-96

NOT APPROVABLE - MINOR

A Trusted Name For Over Half A Century

PUREPAC

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-527-0649

MINOR AMENDMENT

UPS OVERNIGHT COURIER

January 31, 1997

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food & Drug Administration
Document Control Room
MPN II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: ANDA 74-819, Etodolac Tablets, 400 mg

Dear Mr. Sporn:

Reference is made to the December 3, 1996 tentative approval of our Abbreviated New Drug Application for Etodolac Tablets, ANDA 74-819. Further reference is made to our January 30, 1997 submission of draft labeling.

Purepac Pharmaceutical Co. is enclosing twelve (12) copies of the revised insert for Etodolac Tablets. This labeling is identical to the draft labeling which was submitted on January 30, 1997. A side-by-side comparison of our proposed insert with that of the listed drug's, with all differences annotated and explained, has been submitted with our January 30 amendment.

If the draft labeling meets with your approval, please consider this as final printed insert labeling.

If you have any questions concerning this submission, please contact the undersigned at (908) 527-9100, Ext. 211.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Charlene Salmorin
Manager, Labeling Control

/cs

A Trusted Name For Over Half A Century

PUREPAC

ORIGIN

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-527-0649

UPS OVERNIGHT COURIER

TELEPHONE AMENDMENT

November 25, 1996

ORIG AMENDMENT
N/AM

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: ANDA #74-819 Etodolac Tablets, 400 mg

Dear Sir/Madam:

Reference is made to our Abbreviated New Drug Application #74-819 for Etodolac Tablets, 400 mg. Further reference is made to the telephone conversation this afternoon between Ms. Cecelia Parise, of the Office of Generic Drugs, and the undersigned from Purepac.

In accordance with our discussion, Purepac is hereby submitting a revised exclusivity statement for the subject application.

If there are any questions regarding this submission, please do not hesitate to call me at (908) 527-9100, ext. 220.

Purepac Pharmaceutical Co. looks forward to the approval of this abbreviated application.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Elizabeth Trowbridge

Elizabeth Trowbridge, R.A.C.
Manager, Regulatory Affairs

ET:cch
Enclosures

A Trusted Name For Over Half A Century

PUREPAC

ORIGINAL

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-527-0649

559-1599

UPS OVERNIGHT COURIER

MINOR AMENDMENT

December 31, 1996

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: Etodolac Tablets, 400 mg, ANDA #74-819

Dear Mr. Sporn:

Reference is made to our January 31, 1996 submission of an Abbreviated New Drug Application for Etodolac Tablets, 400 mg, ANDA #74-819. Further reference is made to your December 3, 1996 letter stating that this application is tentatively approved.

In accordance with the request in the December 3, 1996 correspondence, Purepac is hereby submitting this Minor Amendment containing updated labeling and chemistry, manufacturing and controls information. The specific modifications incorporated into the revised documents are explained in the appropriate section of this submission. In addition, Section 4 of this amendment contains the required Field Copy Certification.

If you have any questions regarding this submission, please do not hesitate to call me at (908) 527-9100, ext. 220.

Sincerely,
PUREPAC PHARMACEUTICAL CO.

Elizabeth Trowbridge

Elizabeth Trowbridge, R.A.C.
Manager, Regulatory Affairs

ET:cch
Enclosures

RECEIVED
JAN 03 1997
GENERIC DRUGS

1-10-97 Tolline

A Trusted Name For Over Half A Century

PUREPAC

ORIGINAL

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-527-0649

MINOR AMENDMENT

UPS OVERNIGHT COURIER

January 30, 1997

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food & Drug Administration
Document Control Room
MPN II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA ORIG AMENDMENT
N/A

RE: ANDA 74-819, Etodolac Tablets, 400 mg

Dear Mr. Sporn:

Reference is made to the December 3, 1996 tentative approval of our Abbreviated New Drug Application for Etodolac Tablets, ANDA 74-819. Further reference is made to your January 27, 1997 letter requesting labeling revisions.

Purepac Pharmaceutical Co. is amending the above referenced application to include revised draft package insert labeling. Enclosed are four (4) copies of the revised insert for your review. Also enclosed is a side-by-side comparison of our proposed insert with that of the listed drug's with all differences annotated and explained. Final printed insert labeling will be submitted upon your request.

If you have any questions concerning this submission, please contact the undersigned at (908) 527-9100 Ext. 211.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Charlene Salmorin

Charlene Salmorin
Manager, Labeling Control

RECEIVED
JAN 31 1997
GENERIC DRUGS

/cs